What is claimed is:

1. A controlled release composition comprising:

a plurality of solid nano-spheres, each of said solid nano-spheres, said plurality of solid nano-spheres being encapsulated in a pH sensitive or salt sensitive micro-sphere, said pH sensitive or salt sensitive micro-sphere is formed of a pH sensitive or salt sensitive matrix material, and a first active agent incorporated into said solid nano-spheres or said microsphere or in both said solid nano-sphere and said micro-sphere, wherein said first active agent is a nucleic acid.

2. The composition of claim 1 wherein said first active agent is incorporated in said solid nano-spheres and further comprising a second active agent encapsulated in said pH sensitive or salt sensitive matrix material wherein said pH sensitive or salt sensitive matrix material releases said second active agent upon contact with a solution having a predetermined pH or predetermined salt concentration.

3. The composition according to claim 1 wherein said pH sensitive micro-sphere degrades or dissolves when said pH sensitive micro-sphere contacts a solution having a pH in the range of about 3 to about 12.

4. The composition according to claim 1 wherein said pH sensitive or salt sensitive matrix material degrades or dissolves when said pH sensitive micro-sphere contacts a solution having a pH greater than about 5.

5. The composition according to claim 1 wherein said pH sensitive or salt sensitive matrix material is a cationic pH sensitive polymer that is water insoluble at a pH above about 9 water soluble at a pH of about 7 or below.

6. The composition of claim 1 wherein said pH sensitive material is selected from the group consisting of:

acrylate polymers with amino substituents, acrylic acid esters, polyacrylamides, phthalate derivatives and mixtures thereof.

7. The composition of claim 1 wherein said pH sensitive material is selected from the group consisting of:

acid phthalate of carbohydrate, amylose acetate phthalate, cellulose acetate phthalate, cellulose ester phthalate, cellulose ether phthalate, hydroxy propyl cellulose phthalate, hydroxypropyl ethylcellulose phthalate, hydroxypropyl methyl cellulose phthalate, methyl

cellulose phthalate, polyvinyl acetate phthalate, polyvinyl acetate hydrogen phthalate, sodium cellulose acetate phthalate, starch acid phthalate, styrene-maleic acid dibutyl phthalate copolymer, styrene-maleic acid polyvinyl acetate phthalate copolymer, styrene and maleic acid copolymer, gelatin, gluten, shellac, salol, keratin, keratin sandarac-tolu, ammoniated shellac, benzophenyl salicylate, cellulose acetate trimellitate, cellulose acetate blended with shellac, hydroxypropylmethyl cellulose acetate succinate, oxidized cellulose, polyacrylic acid derivative, acrylic acid and acrylic ester copolymers, methacrylic acid, methacrylic acid ester, vinyl acetate, crotonic acid copolymer and mixtures thereof.

8. The composition of claim 1 wherein a first portion of said plurality of nano-spheres are adhered to a second portion of said plurality of nano-spheres with a pH sensitive or salt sensitive matrix material.

9. The composition of claim 1 further comprising a moisture sensitive material mixed with said pH sensitive or salt sensitive material of said micro-sphere.

10. The composition of claim 9 wherein said moisture sensitive material is selected from the group consisting of polyvinyl pyrrolidone, water soluble cellulose, polyvinyl alcohol, ethylene maleic anhydride copolymer, methyl vinyl ether maleic anhydride copolymer, polyethylene oxides, polyamide, polyester, copolymers or homopolymers of acrylic acid, polyacrylic acid, polystyrene acrylic acid copolymer, starch derivatives, polyvinyl alcohol, acrylic acid copolymer, anionic polymer of methacrylic acid and methacrylate, cationic polymer having dimethyl-aminoethyl ammonium functional groups, hydroxyethyl cellulose, carboxymethyl cellulose, hydroxymethyl cellulose, carboxymethyl cellulose, hydroxypropyl carboxymethyl cellulose, hydroxypropyl methyl carboxyethyl cellulose, hydroxypropyl carboxypropyl cellulose, hydroxybutyl carboxymethyl cellulose, polysaccharide, hydrocolloid, natural gum, protein, and mixtures thereof.

11. The composition of claim 1 wherein said pH sensitive material is relatively insoluble and impermeable at the pH of the stomach and is more soluble and permeable at the pH of the small intestine and colon.

12. The composition of claim 11 wherein said pH sensitive material is selected from the group consisting of polyacrylamides, phthalate derivatives such as acid phthalates of carbohydrates, amylose acetate phthalate, cellulose acetate phthalate, other cellulose ester phthalates, cellulose ether phthalates, hydroxypropylcellulose phthalate,

hydroxypropylethylcellulose phthalate, hydroxypropylmethylcellulose phthalate, methylcellulose phthalate, polyvinyl acetate phthalate, polyvinyl acetate hydrogen phthalate, sodium cellulose acetate phthalate, starch acid phthalate, styrene-maleic acid dibutyl phthalate copolymer, styrene-maleic acid polyvinylacetate phthalate copolymer, styrene and maleic acid copolymers, polyacrylic acid derivatives such as acrylic acid and acrylic ester copolymers, polymethacrylic acid and esters thereof, poly acrylic methacrylic acid copolymers, shellac, and vinyl acetate and crotonic acid copolymers.

13. The composition of claim 1 wherein said solid nano-spheres are formed of a wax material has a melting point in the range of between about 25 degrees C and about 150 degrees C.

14. The composition of claim 13 wherein said wax material has a penetration point of about 1 to about 10.

15. The composition of claim 13 wherein said wax material is selected from the group consisting of:

natural wax, synthetic wax, regenerated wax, vegetable wax, animal wax, mineral wax, petroleum wax, microcrystalline wax and mixtures thereof.

16. The composition of claim 13 wherein said wax comprises one or more of carnauba wax, candelilla wax and beeswax.

17. The composition of claim 1 wherein said solid nano-spheres are formed of a fat material is selected from the group consisting of:

hydrogenated castor oil, hydrogenated vegetable oil, hard fat, glyceride, fatty acids, fatty acid derivative, lipid, steroid and mixtures thereof.

18. The composition of claim 17 wherein said glyceride is selected from the group consisting of:

triglyceride, monoglyceride, diglyceride, glyceryl monostearate, glycerol tristearate and mixtures thereof.

19. The composition of claim 17 wherein said fatty acid derivative is selected from the group consisting of:

alcohol, ester, anhydride, hydroxy fatty acid and prostaglandin.

20. The composition of claim 17 wherein said fat material is selected from the group consisting of:

lauric acid, physeteric acid, myristoleic acid, palmitoleic acid, petroselinic acid, oleic acid, isolauric acid, isomyristic acid, isopalmitic acid, isostearic acid, isoprenoid, 12-(((7'-diethylaminocoumarin-3yl)carbonyl)methylamino)-octadecanoic acid, N-[12-(((7'diethylaminocoumarin-3-yl)carbonyl)methyl-amino)octadecanoyl]-2 -aminopalmitic acid, N succinyl-dioleoylphosphatidylethanol amine, palmitoyl-homocysteine, digalactosyldiglyceride, 1,2-dioleoyl-sn-glycerol; 1,2-cdipalmitoyl-sn-3 succinylglycerol; 1,3-dipalmitoyl-2-succinylglycerol and mixtures thereof.

21. The composition of claim 17 wherein said fat material is selected from the group consisting of:

phospholipid, sphingolipid, cholesterol, steroid derivative, terpene, tocopherol, stearlyamine, vitamin and mixtures thereof.

22. The composition of claim 21 wherein said phospholipid comprises:

phosphatidic acid, phosphatidyl choline, phosphatidyl ethanolamine, phosphatidylglycerol, phosphatidylserine, phosphatidylinositol, lysophosphatidyl derivative, cardiolipin, beta-acyl-y-alkyl phospholipid, phosphatidylcholines, dioleoylphosphatidylcholine, dimyristoylphosphatidylcholine, dipentadecanoylphosphatidylcholine, dilauroylphosphatidylcholine, dipalmitoylphosphatidylcholine (DPPC), distearoylphosphatidylcholine (DSPC), diarachidoylphosphatidylcholine (DAPC), dibehenoylphosphatidylcholine (DBPC), ditricosanoylphosphatidylcholine (DTPC), dilignoceroylphatidylcholine (DLPC), phosphatidylethanolamine, dioleoylphosphatidylethanolamine, 1-hexadecyl-2-palmitoylglycerophosphoethanolamine, synthetic phospholipids and mixtures thereof.

23. The composition of claim 21 wherein said steroid is selected from the group consisting of:

cholesterol, cholesterol sulfate, cholesterol hemisuccinate, 6-(5-cholesterol 3 beta-yloxy) hexyl6-amino-6-deoxy-1-thio-alpha-D-galactopyranoside, 6-(5-cholesten-3 beta-tloxy)hexyl-6-amino-6-deoxyl-1-thio-alpha-D mannopyranoside, cholesteryl(4'-trimethyl 35 ammonio)butanoate and mixtures thereof.

24. The composition of claim 1, wherein said micro-sphere further comprises a water sensitive material is selected from the group consisting of:

natural oligomer, synthetic oligomer, natural polymer, synthetic polymer and copolymer, starch, starch derivative, oligosaccharide, polysaccharide, hydrocolloid, natural gum, protein, cellulose, cellulose derivative and mixtures thereof.

25. The composition of claim 1 further comprising a bioadhesive material incorporated into said solid nano-sphere or said micro-sphere or in both said nano-sphere and said micro-sphere.

26. The composition of claim 25 wherein said bioadhesive material is a bioadhesive polymer.

27. The composition of claim 26 wherein said bioadhesive polymer is selected from the group consisting of polyhyaluronic acids, casein, gelatin, glutin, polyanhydrides, polyacrylic acid, alginate, chitosan, poly(methyl methacrylates), poly(ethyl methacrylates), poly (butyl methacrylate), poly(isobutyl methacrylate), poly(hexl methacrylate), poly(isodecl methacrylate), poly(lauryl methacrylate), poly(phenyl methacrylate), poly(methyl acrylate), poly(isopropyl acrylate), poly(isobutyl acrylate), poly(octadecl acrylate) and poly(fumaric-co-sebacic)acid.

28. The composition of claim 1 wherein said nano-sphere further comprises a ligand.

29. The composition of claim 1 wherein said nano-sphere further comprises a targeting material selected from the group comprising lectin viral protein, bacterial protein, monoclonal antibody, antibody fragment, hormone, cell-adhesion molecule, saccharide, drug and neurotransmitter.

30. The composition of claim 1 wherein said first active agent is selected from the group consisting of: an oligonucleotide, oligoribonucleotide, polynucleotide, polyribonucleotide, gene, messenger ribonucleic acid, and ribozyme.

31. The composition of claim 1 wherein said nano-spheres further comprise a cationic surface active agent, anionic surface active agent, a nonionic surface active agent or a zwitterionic surface active agent.

32. The composition of claim 1 wherein said micro-sphere has a size of from about 20 to about 100 microns.

33. The composition according to claim 1 wherein each of said nano-spheres has an average size of about 0.01 to about 5 microns.

34. The composition according to claim 1 wherein said first pharmaceutical active agent is incorporated in said micro-sphere and said nano-spheres and said pH or salt sensitive material upon contact with said solution releases said first pharmaceutical agent to provide a burst and said first pharmaceutical agent is released continuously thereafter for an extended period of time.

35. The composition according to claim 1 wherein the extended period of time is in the range of a day to a period of a few weeks.

36. The composition according to claim 2 wherein upon contact with said solution releases said second pharmaceutical agent to provide a burst and said first pharmaceutical agent is released continuously thereafter for an extended period of time.

37. The composition of claim 1 wherein the composition is formulated in an oral product.

38. The composition according to claim 37 wherein the extended period of time is in the range of a day to a period of a few weeks.

39. An article formed of the composition of claim 1.

40. A composition comprising in combination with a and physiologically acceptable carrier a controlled release composition comprising: a plurality of solid nano-spheres, said plurality of solid nano-spheres being encapsulated in a pH sensitive or salt sensitive micro-sphere, said pH sensitive or salt sensitive micro-sphere is formed of a pH sensitive or salt sensitive matrix material, and a first pharmaceutical active agent incorporated into said solid nano-spheres or said microsphere or in both said solid nano-sphere and said micro-sphere, in a quality sufficient upon administration in a single or multiple does regimen to a mammal to release said first pharmaceutical active agent, wherein said first active agent is a nucleic acid.

41 The composition of claim 40 wherein said composition is administered orally.

42. The composition according to claim 40 in which said dosage form is selected from the group consisting of powder, tablets, capsules, ligand, elixir and granules.

43. The composition of claim 1 wherein said first pharmaceutical active agent is delivered to the gastrointestinal tract.

44. The composition of claim 1 wherein said first active agent is delivered to the stomach and/or small intestine.

45. A method for delivering an active substance to a preselected environment; said method comprising the steps of introducing to said environment a control release composition, said control release comprising: a plurality of solid nano-spheres, said plurality of solid nano-spheres being encapsulated in a pH sensitive or salt sensitive micro-sphere, said pH sensitive or salt sensitive micro-sphere is formed of a pH sensitive or salt sensitive matrix material, and a first active agent incorporated into said solid nano-spheres or said microsphere or in both said solid nano-sphere and said micro-sphere, said first active agent comprising a nucleic acid,

wherein introducing of said composition into said environment permits degradation of said composition and release of said active agent.

46. The method of claim 45 wherein before step a. orally administering said controlled release composition.

47. The method of claim 45 wherein said environment is the stomach and/or small intestine.

48. The method of claim 45 wherein said pH sensitive micro-sphere degrades or dissolves when said pH sensitive micro-sphere contacts a solution having a pH in the range of about 3 to about 12.

49. The method of claim 45 wherein said pH sensitive material is selected from the group consisting of:

acid phthalate of carbohydrate, amylose acetate phthalate, cellulose acetate phthalate, cellulose ester phthalate, cellulose ether phthalate, hydroxy propyl cellulose phthalate, hydroxypropyl ethylcellulose phthalate, hydroxypropyl methyl cellulose phthalate, methyl cellulose phthalate, polyvinyl acetate phthalate, polyvinyl acetate hydrogen phthalate, sodium cellulose acetate phthalate, starch acid phthalate, styrene-maleic acid dibutyl phthalate copolymer, styrene-maleic acid polyvinyl acetate phthalate copolymer, styrene and maleic acid copolymer, gelatin, gluten, shellac, salol, keratin, keratin sandarac-tolu, ammoniated shellac, benzophenyl salicylate, cellulose acetate trimellitate, cellulose acetate blended with shellac, hydroxypropylmethyl cellulose acetate succinate, oxidized cellulose, polyacrylic acid derivative, acrylic acid and acrylic ester copolymers, methacrylic acid, methacrylic acid ester, vinyl acetate, crotonic acid copolymer and mixtures thereof.

50. The method of claim 45 wherein a first portion of said plurality of nano-spheres are adhered to a second portion of said plurality of nano-spheres with a pH sensitive or salt sensitive matrix material.

51. The method of claim 45 further comprising a moisture sensitive material mixed with said pH sensitive or salt sensitive material of said micro-sphere.

52. The method of claim 45 wherein said active agent is selected from the group consisting of: an oligonucleotide, oligoribonucleotide, polynucleotide, polyribonucleotide, gene, messenger ribonucleic acid, and ribozyme.

53. The method of claim 45 wherein said active agent is delivered to the stomach and/or small intestine.

54. The method of claim 45 wherein said active agent is delivered to the gastrointestinal tract.

55. The method of claim 45 further comprising a bioadhesive material incorporated into said solid nano-sphere or said micro-sphere or in both said nano-sphere and said micro-sphere.

56. The method of claim 45 wherein said bioadhesive material is a bioadhesive polymer.

57. The method of claim 45 wherein said nano-sphere further comprises a ligand.

58. The method of claim 45 wherein said nano-sphere comprises a targeting material selected from the group comprising lectin viral protein, bacterial protein, monoclonal antibody and antibody fragment.

59. A process for producing the multi component controlled release system comprising the steps of:

heating a hydrophobic material to a temperature above the melting point to form a melt;

dissolving or dispersing the first active agent into the melt;

dissolving or dispersing a second active agent, and the pH sensitive matrix, in the aqueous phase and heating it to above the melting temperature of the hydrophobic material;

mixing the hot melt with the aqueous phase to form a dispersion;

high shear homogenization of the dispersion at a temperature above the melting temperature until a homogeneous fine dispersion is obtained;

cooling the dispersion to ambient temperature; and